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ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE

DISEASES OF INFANTS AND CHILDREN

JOHN FITCH LANDON, M.D., Editor

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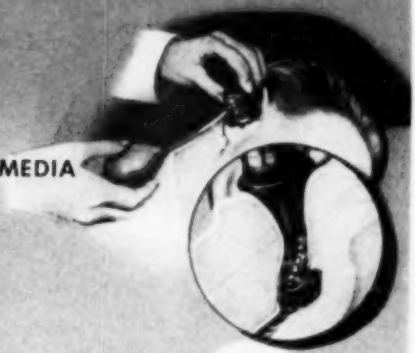

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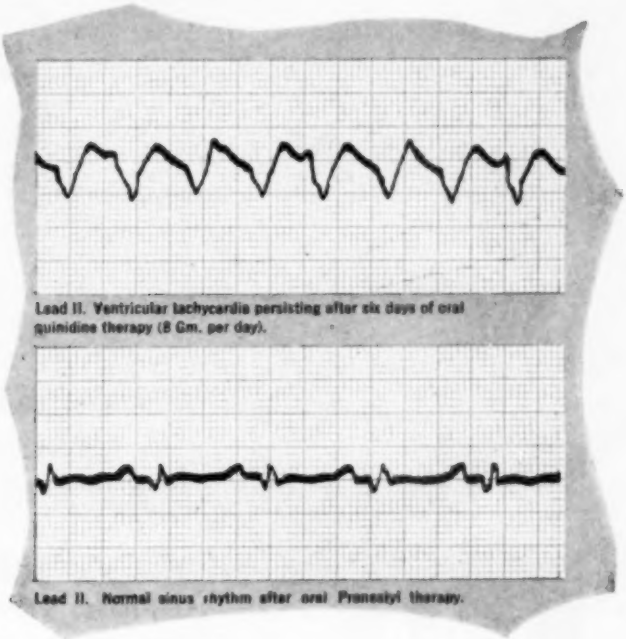

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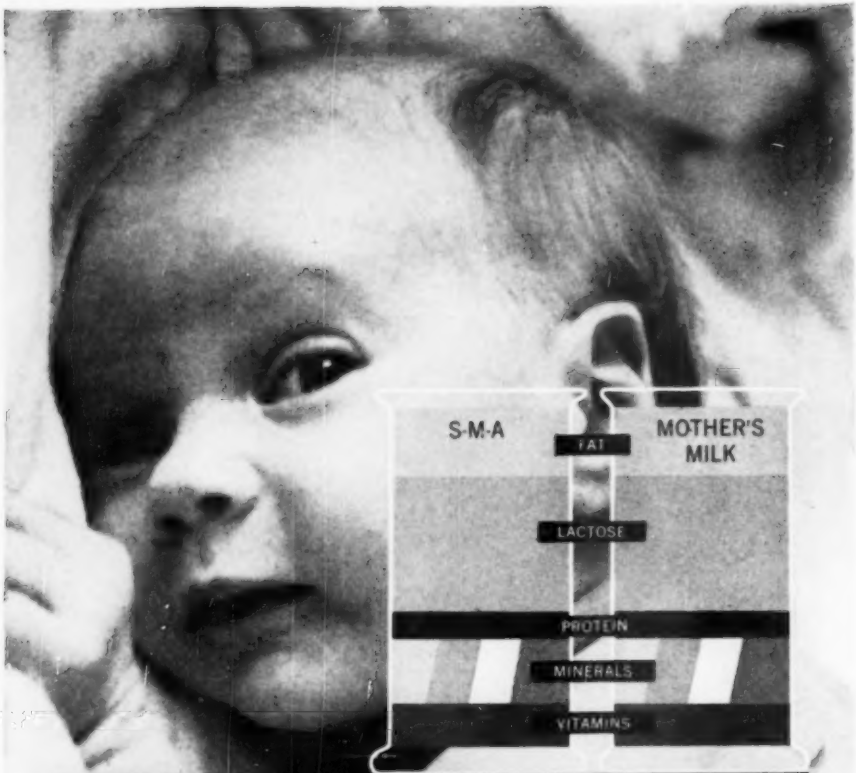

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1. *Reeb, R. B., Rohr, J. R., and Colwell, A. R.: Proc. House Staff Dept. Med., Wesley Memorial Hospital, Chicago, Ill. Feb. 6, 1946.*

2. *Rohr, J. H., and Colwell, A. R., Proc. Amer. Diabetes Ass. 6:37, 1946.*

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DIPHTHERIA REVISED*

J. C. GEIGER, M.D.

AND

M. S. MARSHALL, Ph.D.

San Francisco.

The story of diphtheria has long been one of the most satisfying chapters in the textbook of medical bacteriology. There is one organism, the diphtheria bacillus, at least not yet subdivided into too many types. Infection is direct, from cases or identifiable carriers to potential cases or carriers, by recognizable routes. The organism remains localized and produces an infection in an area which can be seen and cultured, without concern over whether or not it may cause an abscess in the liver, a meningitis, or some other metastatic infection. There is more or less intoxication which, combined with infection, produces a disease the pathology of which is not abstruse. Specimens for bacteriologic examination are simple; laboratory techniques are available and laboratories report that organisms resembling the diphtheria bacillus were or were not found, and, later, that the culture was or was not virulent. Epidemiologically there are cultures, the Schick test to separate susceptible from immune persons, toxoid to immunize those found to be susceptible, and antitoxin to neutralize the toxin of those with toxic diphtheria. The picture of diphtheria in the textbook is drawn with the sharpness of a steel engraving.

In recent years there have been epidemiologic mutterings about

*From the University of California Medical School, San Francisco, and the San Francisco Department of Public Health.

diphtheria. It has too often failed to follow the textbook. The principal objectors have been clinicians, to whom the disease itself transcends the bacteriologic textbook, and epidemiologists, who have been disturbed by the lack of accord between the textbook and the facts. The objections have been of two principal sorts. One refers to the character of the disease itself and the other to the immunity to diphtheria.

It has been claimed that the character of the disease has become sometimes unexpectedly severe, refractory to treatment under what appeared to be satisfactory conditions. There appears to have been some drift toward occurrence in older age groups.[1] To these observations there have been theories expressed, but nothing more. For example, the subdivision of the diphtheria bacillus into *gravis, mitis,* and two less definite types has been used in an effort to blame clinical and epidemiologic changes on possible changes in the bacillus itself. Whether or not this is a factor, it is an inadequate explanation. It has been said that an associative growth, presumably with streptococci, accounts for the severe and unresponsive character of the disease in some outbreaks or cases. This is not at all substantiated, though again it might be a mistake to say that it never occurs. It has been said that widespread immunization has so altered the immunity to diphtheria and the distribution of the bacillus that the whole character of the disease has been changed. This cosmic idea is a bit speculative; at least it would be difficult to prove and is difficult to support except as another possible contributing factor. Whatever the reasons, that diphtheria is not always as neatly responsive to treatment as the rules seem to demand seems unequivocal. There is a discrepancy between textbook and fact in characterization of the disease.

In immunity, objections to the textbook can be made on unassailable grounds. Persons whose Schick tests are negative do come down with diphtheria fairly frequently. Persons whose Schick tests are positive can become healthy carriers for long periods without succumbing to the disease. As many as one-third of the cases admitted to hospitals during an outbreak of diphtheria may have been previously immunized by accepted methods.[2,3] These observations are consistently related to the amounts of antitoxin present, sometimes spectacularly so; that is, a person with diphtheria and negative to the Schick test may have not just a little

more than the threshold amount of antitoxin but a great deal of antitoxin. Persons who become carriers, though they are positive to the Schick test and have little or no antitoxin, may take care of patients or be relatives of patients.[3] These discrepancies are no fuzzy errors at the borderlines of measurements; they are precisely opposed to the ideas of the textbook and, since they cannot be denied as facts, they must be met by revision or reconsideration of the textbook. It has either been wrong for a long time or we have not read it correctly.

In going back to the textbook to give it a fair trial before condemnation, the only change found to be necessary is one of viewpoint. The literal facts of the textbook are still facts; the newer knowledge of diphtheria also deals with facts. Only the viewpoint of the textbooks has been misleading us.

Diphtheria is known to be an infection and also an intoxication. Neither the mechanisms nor the consequences of these two processes are confusing. Bacteriologically, the diphtheria bacillus has two separate and independent qualities which, when they coincide, do so only by accident. A diphtheria bacillus can be infectious, meaning that it can establish itself and grow, and still be a poor producer of toxin, at least by all the criteria that we have. The old Park No. 8 strain of the diphtheria bacillus, on the other hand, both by test and by experience is a good potential producer of toxin and yet it is conceded to have lost much of its power to infect if, indeed, this power ever was high with this strain.[4] After all, a power to infect indicates an ability on the part of a microorganism to utilize or to adapt itself to a warm moist environment and live on the secretions, the debris from cells and food, and the interstitial fluids, in the presence of such inhibiting substances as may be present. There is no reason to suppose that this should be in accord with the particular metabolic activity which brings about the synthesis of a specific substance, the toxin, any more than all strains of species of bacteria which produce pigments always produce equal amounts. This concept of diphtheria bacilli is in accord with history, with the textbooks, with the evidence in the disease itself, and with modern viewpoints.

At this point in the chapter on diphtheria there is a transition from the recognition of infectiousness and toxigenicity as unrelated qualities of the diphtheria bacillus to a viewpoint that the disease

is only an intoxication. The textbooks have oversimplified a part of the story of diphtheria, though the evidence against such simplification has been constantly before us. The question is asked, "Who is immune to diphtheria?" In answer, it is proposed that we find out by discovering who has more and who has less than a given concentration of antitoxin in their blood. Antitoxin is given to patients, or toxoid is injected so that antitoxin may be formed. These moves ignore entirely the fact that diphtheria is primarily an infection and secondarily an intoxication, from the standpoint of pathogenesis. The clinical importance of intoxication does not give it a secondary position, but the development of the disease demands that there be a major infection before there can be serious intoxication.

The Schick test is only a test for a threshold level of antitoxin. It has never been more. Where the threshold is or should be may be equivocal, but the principle is clear. The test has been used for over thirty years with fair success, meaning that relatively few persons whose reactions were thought to be positive became carriers instead of acquiring the disease, and most of those who did not react to the Schick test did not get the disease on apparent exposure. Now we add to our data; a good many cases of diphtheria occur among negative reactors and a significant number of carriers have been found among the positive reactors. Having revised the viewpoint to include infection, this would be expected. There appear to be a number of strains of diphtheria bacilli which are relatively high in infectiousness but relatively inactive in toxigenicity. These strains, in contradistinction to those high in toxigenicity or high in both qualities, would tend to produce carriers and might well not produce toxin in all persons in quantities upsetting to those whose Schick tests were positive. In the avowed absence of antitoxin, it might almost be argued that something of this sort must be so, particularly if there is some resistance to infection itself. Conversely, a strain of diphtheria bacilli exceptionally active in the production of toxin might and apparently can overwhelm a person reacting negatively to the Schick test, for the level of that test in terms of neutralization is low. This would be particularly true with strains of diphtheria bacilli high in infectiousness as well as active in the production of toxin, for these strains would be not only active in the produc-

tion of toxin but they would be producers on a large scale because of the activity of their infection.

The fact that the Schick test has been fairly successful and that only relatively recent data have upset it might suggest that there has been a shift in strains of the diphtheria bacillus to a group with new characteristics but this borderline fantasy is not needed. By supposing what is a virtual certainty, that diphtheria bacilli may be either high or low in infectiousness and also in toxigenicity, there may be low-low, low-high, high-low, and high-high combinations. These would, of course, merge in continuous series, but the use of the relative terms, high and low, permits a categorical approach. It is reasonable to suppose that most strains of diphtheria bacilli share the two qualities in fair level. This would make the Schick test a reasonable tool, yet discrepancies should be expected because of the existence of strains with unbalanced combinations. Whether infectiousness or toxigenicity of diphtheria bacilli are correlated with *gravis* and *mitis* types are matters still to be studied. Correlation of the known features of these types with infectiousness and toxigenicity is not only a matter of conjecture; since infectiousness and toxigenicity are separate, close correlation seems unlikely. There is no satisfactory technique for measurement of infectiousness; toxin or antitoxin levels are only part of the story of toxigenicity.

A discussion of apparent discrepancies between levels of antitoxin and resistance to infection simply clarifies the need for differentiation between the two. The Schick test measures, not too accurately, a level of antitoxin, and rather a low one, probably between 0.1 and 0.002 of a unit per milliliter of serum at the threshold of reaction.[5] That is, nonreactors presumably have at least more than 0.002 unit and the reactors presumably have at least less than 0.1 unit. Titration of the amount of antitoxin instead of performing the Schick test changes nothing in the argument except that it is then possible to speak more accurately of the toxin-neutralizing capacity of the serum of a person tested, still without regard to the capacity of the organism to infect or the person to resist infection. For this latter immunologic balance there is no measuring stick. Let the capacity of an organism to infect be laid out on a scale, say 1 to 100, and the capacity of persons to resist infection be similarly laid out, and this appears

to be an unmeasured but real factor in diphtheria that can hardly be denied.

Toxoid, in the same way, is designed to meet needs arising from the toxigenicity of diphtheria bacilli. Toxoid produces various antitoxic responses in persons injected. Some develop large concentrations of antitoxin readily and either maintain them for long periods or later respond actively to the slightest stimulus. Other persons respond poorly and perhaps become positive to the Schick test a year or two later, or even fail ever to develop a negative reaction. Beyond possible equivocation, following toxoid the antitoxin content of persons, or their responsiveness to stimuli, is variable.[8] All this, however, is in terms of antitoxin. The role of infectiousness still has to be considered. Therefore, it is reasonable to suppose that many persons who have had toxoid can also have diphtheria. Have not textbooks said clearly for many decades that an attack of diphtheria need not leave an immunity to a subsequent attack? Why, then, should there be any surprise when as many as a third of the patients are found to have had previous toxoid? And why should there not be such a thing as a fair immunity to infection without antitoxic immunity? The error is not in the textbook so much as in our naïve simplification of the story.

The quality of "virulence" is of more basic interest to bacteriologists than to clinicians, but tests are often requested and belief in the results is widespread, just as is belief in the simplified immunologic approach. The virulence test is a good example of the manner by which observers have lost sight of infectiousness in so closely relying upon toxigenicity. This is not the place to discuss the various techniques for virulence tests, the use of whole cultures versus the use of pure cultures, the lethal test, the dermal tests done with two or one guinea pigs, the rabbit test, the chick test, or the plate test. Under the principles now discussed, however, the virulence would have to include both infectiousness and ability to produce toxin. None of the so-called "virulence tests" make a clear distinction.

Methods by which a "virulent" strain kills an animal presumably require that the organisms establish a firm beachhead at a point of inoculation and develop toxin, which is the lethal agent. Dermal reactions are essentially inflammatory, and inflammation can be produced either by toxin or by the growth of the organisms as in-

fecting agents. This, the most frequent type of test, is not distinctive. The plate test, now finding some favor because it requires no animals, is not only solely a test of the ability of a tested strain to produce toxin but that ability is tested under abortively artificial conditions. "Virulence" tests, in short, are artificial, indistinct, and often incomplete. The present point is not to disqualify virulence tests, which, like the Schick test, probably have a useful though incomplete correlative value, but to indicate the unfortunate ease with which infectiousness and toxigenicity are normally mixed up without actually denying the existence of either quality.

The fact that persons who have been inoculated with toxoid are not as likely to die and that they respond better to antitoxin is not only consistent with the interpretations given but is a fortunate support to the efforts that have been made to immunize young persons. Those who respond poorly, those who lack any resistance to infection itself, or those who encounter unusually infectious organisms are likely to have diphtheria later on exposure. The Schick test, if used as a measure of responsiveness or as a partial measure of safety, adequate for some but not for all, may well also have its uses, but its limitations must be recognized. Measurement of specific levels of antitoxin, an arduous and expensive task, does not now nor ever has served any purpose except for investigations.

A revised viewpoint, one which demands no new concepts, enables the thoughtful health official to approach diphtheria control without radical change, yet the clarification gained by enlarging the story so that response is measured in terms of infection as well as antitoxin puts the rationale of preventive procedures on a much firmer footing.

Toxoid has been advocated for preschool children and for children in their early school years. The evidence still warrants this as a move which will reduce the number of cases and the number of serious or fatal cases, all else being equal. Schick tests have not been advocated in schools, because of their cumbersomeness more than because of lack of faith in them. Now perhaps that can be dropped for reasons of lack of faith, except under very special circumstances.

With specific outbreaks, the changed viewpoint becomes more conspicuous. Immunized persons may acquire diphtheria, persons negative to the Schick test may acquire the disease, and positive

reactors may be carriers. This alters somewhat the handling of infectious disease wards and epidemics by taking away some of the tools. However, the tools have not been good ones; they have too often failed. Discrepancies are not expected. Recognition of diphtheria as a twofold disease, an infection and an intoxication, removes the discrepancies. The diphtheria bacillus should always be considered as an organism high or low in either infectiousness or toxigenicity, just as patients or persons should be thought of as high or low in refractoriness either to infection or to intoxication, possibly but not necessarily both.

The intoxication is the only part of the disease to which the Schick test, toxoid, and antitoxin apply. The "virulence test" must be viewed with some skepticism. This test is not as useful as is commonly supposed. It takes from three days to a week to perform. Usually this is useful only for the records, a basis of laboratory work often open to considerable criticism. Virulence tests are probably positive for frankly toxigenic strains, and such strains appear to compose a fair fraction of all of those strains of diphtheria bacilli active in the epidemiology of the disease. Otherwise the platform of protective procedures would have collapsed long since. However, epidemiologists and all who deal with diphtheria need to realize that the virulence test may be uncertain with those infectious organisms which lack any marked ability to produce toxins, just as the Schick test and toxoid are partial props on which it is unwise to rely too strongly.

Warm tribute is herewith given to the remarkable British monograph[2] produced by Dr. Percival Hartley and those associated with him, reporting on studies of outbreaks at Newcastle and at Gateshead. The discussions herein antedate this recent monograph by many years, but there could hardly be a more beautiful exposition of the discrepancies between the whole facts and the dogma that has grown up with regard to diphtheria.

REFERENCES

1. Dauer, C. C.: Trends in Age Distribution of Diphtheria in the United States. U. S. Pub. Health Repts., 65: 1309, 1950.
2. Hartley, Percival, et al.: Spec. Rept. 272, Brit. Med. Res. Council, 1950.
3. Galbraith, T. W.; Fraser, R. S. and Bramhall, E. H.: Appearance of Minimus Type of C. Diphtheriae in Utah. U. S. Pub. Health Repts., 63: 577, 1948.
4. Frobisher, M. and Parsons, E. L.: Studies on Type-specific Immunization with Somatic Antigens of C. Diphtheriae. Am. J. Hyg., 52: 239, 1950.
5. Marshall, M. S.: The Borderline Schick Test. J. Pediat., 37: 630, 1950.
6. Marshall, M. S.: Immunity in Diphtheria. California & West. Med., 37: 126, 1932

FIFTY SYMPTOMS OF CHRONIC SINUSITIS IN CHILDREN

With Differential Diagnosis of Each Symptom

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Sinus-conscious pediatricians recognize sinusitis as a focus of infection in children responsible for most of their symptoms during the colder months of the year. The most gratifying experience of a physician is to be successful in treating the many complaints of children, previously handled symptomatically because sinusitis was not recognized as the cause.

Fifty symptoms of chronic sinusitis are discussed in this paper. Some of these symptoms were previously noted under twenty-two signs (objective symptoms).[1] Where a symptom occurs in diseases other than sinusitis, these diseases are given in the differential diagnosis.

The fifty symptoms are: 1. Frequent or prolonged colds. 2. Catarrh or postnasal mucopus. 3. Sniffing. 4. Hacking. 5. Nasal discharge. 6. Nasal obstruction. 7. Mouth breathing. 8. Snoring. 9. Anorexia upon arising. 10. Nausea and/or vomiting upon arising. 11. Malnutrition. 12. Sneezing upon arising in cool weather. 13. Fetor oris upon arising. 14. Headaches upon arising. 15. Low-grade fever. 16. Fatigue. 17. Recurrent tonsillitis. 18. Recurrent pharyngitis. 19. Otitis media. 20. Mastoiditis. 21. Tinnitus. 22. Vertigo. 23. Progressive deafness. 24. Cough and expectoration. 25. Laryngitis. 26. Bronchitis. 27. Infectious (bacterial) asthma. 28. Recurrent pneumonia. 29. Bronchiectasis. 30. Photophobia and "squinting." 31. Pain back of eyes. 32. Conjunctivitis. 33. Picking at nose. 34. Epistaxis. 35. Anosmia. 36. Nervousness. 37. Grinding of teeth. 38. Pavor nocturnus. 39. So-called "habit spasms." 40. Chorea. 41. Night sweats. 42. Rheumatic pains. 43. Abdominal pain. 44. Purpura hemorrhagica. 45. Momentary head pain caused by cold foods. 46. Ill effects of prolonged recumbency. 47. Menorrhagia, metrorrhagia and dysmenorrhea. 48. Convulsions. 49. Recurrent pyelitis and nephritis and 50. Onychophagia. Each symptom is discussed, including differential diagnosis.

1. FREQUENT OR PROLONGED COLDS are invariably associated with chronic sinusitis.[2-8] Crooks and Signy[5] found frequent colds present in 83 per cent of 100 children with sinusitis. Frequently recurring colds are exacerbations of chronic sinusitis caused by the streptococcus.[8] That they are not caused by a virus is evident for three reasons: (1) Virus colds produce an immunity of three[9] to six[10] months or longer, during which time many children may have several colds.[8] (2) Bacteriostatic agents, taken prophylactically, reduce the incidence of colds,[11,12] a result not to be expected against a virus. (3) Finally, since colds affect millions of people almost simultaneously throughout the country during chilling weather,[13-16] a virus would have to be present in the nose or throats of these individuals before chilling could produce a cold. Such a virus has never been found; the streptococcus has.[8]

Differential Diagnosis: a. tonsils and adenoids; b. "summer colds" (allergy).

a. *Tonsils and Adenoids* have no relation to frequent or prolonged colds. Tonsillectomy neither prevents colds nor lowers their incidence.[17]

b. *"Summer Colds"* are often allergic colds (hay fever). They persist during the pollen season, ceasing in cold weather.

2. CATARRH OR POSTNASAL MUCOPUS is synonymous with sinusitis, the bulk of the mucopurulent secretion emanating from the sinuses.[18,19] Crooks and Signy found that 84 of 100 children with sinusitis had either an anterior or posterior discharge. The "catarrh" is most easily demonstrable upon arising, particularly in the colder months. It causes the hack or cough associated with sinusitis. Reisman[20] points out that Maxson,[21] as far back as 1861, described the symptoms of catarrh, the same symptoms we now recognize as sinusitis.

3. SNIFFING. Sniffing is a lazy way of handling catarrh. Sniffing converts an anterior into a posterior discharge.[5] Among 100 rheumatic children with chronic sinusitis, sniffing was encountered in the absence of an admitted cold in 49 per cent.[22] Osler[23] writes: "In winter nearly all the school children in England have the 'snuffles'."

Differential Diagnosis: a. habit; b. "allergic salute"; c. foreign body in nose; d. congenital syphilis.

a. *Habit.* Sniffing almost invariably diminishes in the summer

months, unless there is an associated allergy, thus ruling out habit. Sniffing is usually followed by hacking and swallowing, suggesting the purposeful attempt to clear the nose of excessive secretions.

b. *"Allergic Salute."* The "allergic salute" described by Bowen and Balyeat[24] is a nose-rubbing and simultaneous sniff. An allergic child with active sinusitis may clear his nose by this maneuver.

c. *Foreign Body in Nose* is a rare cause of sniffing.

d. *Congenital Syphilis* may produce "snuffles." It is encountered in infants along with other syphilitic stigmata.

4. HACKING. Children tend to swallow their postnasal discharge and never hack as violently as do adults. Crooks and Signy describe the symptom as varying from a throat-clearing to a more violent cough, and found it present in 82 per cent of 100 children with sinusitis. Among 100 rheumatic children with chronic sinusitis, we found an audible hack, in the absence of an admitted cold, in 62 per cent.[22] Mezz[25] believes that a hacking cough is a clue to a latent sinusitis. The dry, hacking, chronic cough of chronic sinusitis can hardly be mistaken for anything else.[26, 27]

Seasonal variation in sniffing and hacking was determined by observation of the same patients over a period of years. It was found to be greater in the spring than in the fall. Among 54 rheumatic children with chronic sinusitis, upon whom notations were made regarding sniffing, hacking and postnasal mucopus, both in the fall (October) and spring of the year, observations were recorded at the Cardiac Research Clinic of the New York Post-Graduate Hospital as follows:

Sniffing		Hacking		Postnasal Mucopus	
Fall	Spring	Fall	Spring	Fall	Spring
13	42	17	46	12	35

The above incidence of sniffing, hacking and postnasal mucopus was considered positive only in the absence of a known or admitted cold. The incidence would be considerably greater, particularly in the spring, if these symptoms were recorded also during colds.

Differential Diagnosis: a. habit.

a. *Habit* as a cause of hacking can be ruled out by noting that the hack occurs mainly with acute exacerbations of sinusitis, as

during colds. Hacking of sinusitis is minimal during the summer months; if improvement occurs at this time, habit is ruled out.

5. NASAL DISCHARGE. This takes three forms: (1) the normal, (2) the allergic, and (3) the purulent. A normal, thin, watery, serous secretion is seen if the body is chilled. The allergic and the purulent discharges are abnormal. The allergic is a thin, watery, colorless, profuse, sero-eosinophilic discharge of high pH (alkaline), frequently associated with sneezing and ocular symptoms. Purulent or mucopurulent discharge consists of neutrophilic leukocytes and is thick, colored, viscid, irritating, and of low pH (acid).

Crooks and Signy found nasal discharge, anterior or posterior, in 84 per cent of 100 children with sinusitis.

6. NASAL OBSTRUCTION. In active chronic sinusitis, one nostril or the other may stop up.[6, 19, 25] A shifting nasal obstruction is the rule in pansinusitis, the dependent nostril occluding. Upon reversing the position in bed, so that the obstructed side is uppermost, this nostril soon opens while the dependent nostril tends to close.

McKenzie[26] finds that "nasal obstruction accompanies about 50 per cent of cases of chronic sinusitis." Among 100 rheumatic children with chronic sinusitis, we found partial nasal obstruction, in the absence of a known or admitted cold, in 27 per cent.[22]

McKenzie lists the following causes of nasal obstruction: "Deflected septum, very thick, tenacious discharge, swelling of the nasal mucous membrane and turbinates, polyp formation, or a combination of any or all of them."

Allergy may occlude both nostrils. The type of allergy is variable, perhaps hay fever being the most common. Ingestion of fish or other potential allergens may immediately fill the sinuses and nose.

Foreign body in the nose of children causes a unilateral nasal obstruction of sudden onset.

Complete stenosis of one or both nostrils in young patients is never due to adenoids.[29] Leathart[30] finds that nasal obstruction is more frequently caused by sinusitis than by a large adenoid mass. Among 41 children who had been adenotonsillectomized, 22 still suffered from nasal obstruction.[5] Other, but less common, causes for nasal obstruction are menses[31] and emotional upsets.

7. MOUTH BREATHING. The powerful urge to breathe through

the nose is seen in all individuals, but it is most marked at birth.[32] Infants fight and squirm when their nostrils are obstructed, especially when attempting to suckle.

Chronic sinusitis is the most common cause of mouth breathing in children (Figs. 1, 3, 6, 7). Mouth breathing is often not corrected by removal of adenoids since it is usually due to nasal obstruction (Fig. 1). The so-called "adenoid facies" may be more correctly labeled "sinus facies."[5, 33]

Crooks and Signy found mouth breathing and snoring in 62 per cent of 100 children with chronic sinusitis. Their average age was 7½ years; 41 had their tonsils and adenoids removed and 22 of

Fig. 1. Mouth breathing secondary to chronic sinusitis; tonsils and adenoids absent. Note photophobia. Patient snores and complains of vertigo on motion.

these still suffered from nasal obstruction. The role of sinusitis in mouth breathing is proved by the effectiveness of astringent nose drops.[34, 35, 36]

Differential Diagnosis: a. adenoids; b. deviated septum; c. foreign body.

a. *Adenoids* in infants and young children, up to the third year of life, may cause mouth breathing. Beyond this age adenoids rapidly lose their significance, and in adult life adenoids sufficient

to cause obstructed breathing are a rarity. Old children are often accused of adenoid breathing, when in reality they suffer from sinusitis. Many mouth breathers have had repeated adenoidectomy without benefit.[5, 27]

b. *Deviated Septum* may be due to trauma, heredity, and to unequal development of adjacent bones producing asymmetry found also in other parts of the face. Markedly deviated septa, sufficient to cause nasal obstruction, may produce mouth breathing. Because of poor aeration and drainage, the sinuses on the affected side invariably become infected and aggravate the obstruction.

c. *Foreign Body* in the nose is a rare cause of nasal obstruction and mouth breathing. It is suspected in young children who have a foul-smelling discharge, often blood-tinged, unilateral, with nasal obstruction on the same side.

8. SNORING. Snoring in children is usually dependent on nasal obstruction of sinusitis. The child snorer (Fig. 1) does not develop into the adult type unless there is persistent nasal obstruction.[24]

At least partial mouth breathing is a requisite for snoring.[24] Snoring is involuntary and stops as soon as consciousness is regained. With the mouth open during sleep, the uvula and tonsillar pillars become relaxed. The vibrating part in a snore is the thin edge or velum of the posterior faucial pillars.[25] Habitual mouth breathing or snoring is presumptive evidence of chronic sinusitis.[2, 3, 5, 27]

9. ANOREXIA UPON ARISING. Anorexia in children is a very common complaint of anxious parents. Schultz[26] concludes: "There is no question that focal infections located about the head are by far the major cause of organic anorexia in the child." Of all head foci, only chronic sinusitis causes perpetual anorexia upon arising. In a survey of 150,000 high school students, 18 per cent of girls and 9 per cent of boys ate no breakfast at all.[27]

The anorexia may vary from a mild distaste for food on arising to nausea and vomiting. It may be attended with abdominal pain upon eating. The anorexia improves one or two hours after arising, after swallowed purulent secretions leave the stomach. Anorexic children whose breakfasts are forced sometimes vomit on their way to school or in the classroom. This is particularly true in severe weather.

Differential Diagnosis: a. tuberculosis

a. *Tuberculosis* produces an anorexia for all meals.

10. NAUSEA AND/OR VOMITING UPON ARISING. Several symptoms in sinusitis are more pronounced in the morning. These symptoms are sniffing, hacking, hawking, and are often immediately followed by nausea and vomiting. Part of the nausea and vomiting may be due to the gag reflex produced by purulent secretions in the nasopharynx. Nausea also takes place when pus reaches the stomach. Food urged upon children with active sinusitis may result in vomiting, not only of the food, but of the mucopurulent contents in the stomach.

Appetite returns an hour or two after arising when the bulk of the mucopus has passed from the stomach. If more pus is swallowed, as in active sinusitis or with a cold, nausea may continue.

Differential Diagnosis: a. migraine.

a. *Migraine.* Periodic attacks of migraine are accompanied by nausea and vomiting. Cyclic vomiting in young children is the forerunner of migraine. Attacks of vomiting usually occur early in the morning, before breakfast has been taken. The preceding meal may be regurgitated in undigested form. Nausea and vomiting are more prolonged in migraine than in sinusitis. Attacks may last a day or two.

11. MALNUTRITION. Malnourished children frequently have active chronic sinusitis. McKhann[28] states that chronic upper respiratory infections, especially when associated with postnasal drainage, constitute the major difficulty in infants found to be undernourished. However, sinusitis seldom causes malnutrition unless the infection is severe and prolonged.

McKhann lists less common causes of malnutrition in infants as allergy, congenital malformations and metabolic diseases, such as celiac syndrome and glycogen storage disease. Other causes include insufficient food, an unbalanced diet and avitaminosis.

12. SNEEZING UPON ARISING IN COOL WEATHER. In the colder months, children with active sinusitis tend to sneeze upon arising if the room is not warm. Following chilling, bacterial quickening occurs. Toxins are produced which irritate the nasal mucous membrane. Sneezing may be nature's effort to get rid of the offending organisms and their toxins. Holding[29] believes that we are warned of the onset of a cold by the sneeze, "which notifies us

that chilling of the body or direct irritation has reacted in the nasal mucous membranes through the sympathetics." If the chilling continues, streptococcic activity may continue to the point of producing a cold. If the chilling is only momentary, sneezing ceases and bacterial activity likewise stops.

Differential Diagnosis: a. allergy; b. chilling.

a. *Allergy.* In the colder months, sneezing upon arising must not be blamed on feathers, house dust, or any other supposed antigen in the room. As one observer states: "The concentration of house dust in the air at that time is no different from any other time or certainly no different from what it has been during the night when the patient has been relatively free from symptoms."[40]

b. *Chilling* per se may produce sneezing. This becomes increasingly more common with advancing age when basal metabolic rates lower.

13. FETOR ORIS UPON ARISING. Bad breath upon arising is a common complaint of parents of affected children, although it is seldom detected by the physician. However, in older children, the fetor may be noted in the doctor's office. In such cases mucopus may sometimes be seen clinging to the pharynx.

Fetor oris is almost invariably due to bacterial fermentation. This may result from faulty mouth hygiene, due to retained food particles or their decomposition products,[41] gingivitis, tonsillitis and sinusitis. In stomatitis, Vincent's angina, early scarlet fever, etc., where lesions are produced in the oropharynx, the fetor continues only until the disease has run its course.

Differential Diagnosis: a. constipation; b. tonsils; c. gingivitis; d. bronchiectasis and other respiratory disease; e. hemic.

a. *Constipation* is popularly thought to be the cause of bad breath. This is one of the most common fallacies in medicine.[42] Correction of constipation does not relieve the fetor.

b. *Tonsils*, when infected, are common sources of fetor. After their first invasion by bacteria in early life, tonsils become a fertile culture medium for germs. Following tonsillectomy, fetor may disappear completely; if not, sinusitis should be suspected.

c. *Gingivitis* produces a strong fetor for the duration of the disease.

d. *Bronchiectasis, Pulmonary Tuberculosis and other Respiratory Diseases* may produce constant fetor emanating from the re-

cesses of the bronchi or from the lung parenchyma. Since the fetor is exhaled from the respiratory tract, it cannot be ameliorated by eating or drinking, as is the case in sinusitis or tonsillitis where bacteria and their ferments may be washed down.

e. *Hemic.* We are all familiar with the odor of garlic, acetone and other volatile aromatic substances which are exhaled after being absorbed into the blood stream.[42, 43, 44]

14. HEADACHES UPON ARISING. Crooks and Signy noted frontal headaches in 44 per cent of 100 children with sinusitis at an average age of 7½ years. Sinus headaches tend to occur on arising or after a nap.

That headaches have innumerable causes there can be no doubt. Headaches occur in all toxemias, in convulsions, eye-strain, constipation, brain tumor, hunger, excessive fatigue, emotional tension and may be a signal of mental or physical derangement.

Differential Diagnosis: a. migraine; b. eye strain; c. rheumatism; d. allergy.

a. *Migraine* causes a violent headache and, like sinusitis, is most likely to occur upon arising. However, migraine usually awakens the child before his customary hour of arising; in contrast, sinus headaches are worse upon prolonged recumbency.[45] One nine-year-old child awakened with a migraine attack at 5 A.M., although her parents had set the alarm clock for six o'clock with instructions for the child to look after herself. The responsibility placed upon the child produced a severe headache and vomiting.

Attacks of migraine may occur in the afternoon or evening; this is seldom true in sinus headaches.

Migraine attacks occur in all seasons; sinus headaches ameliorate in warm weather.

b. *Eye Strain* may cause headache after excessive reading or because of refractive errors. Such a headache is relieved by rest of the eyes and is not present, as in sinusitis, upon arising.

c. *Rheumatism* causes headaches, sometimes violent in nature.[46] They occur during recumbency, and are at their worst when fever is present. These headaches are probably caused by sinusitis, present in all rheumatic children.[22]

d. *Allergy* may cause an edema of the brain with resultant headache, usually within a few hours after ingestion of an allergen. Some migraine headaches and many sinus headaches have an allergic basis.

15. LOW-GRADE FEVER is the rule in active chronic sinusitis in children. Chronic low-grade fever in sinusitis is caused by the streptococcus and its dissociants.[17] The fever is dependent on a number of interrelated factors, among which are: amount of infection at the moment, virulence of the organism, degree of patient's immunity at the time, ease of drainage from the sinuses (in turn dependent upon congestion, polyps, deformities of septum), and resultant degree of cervical and submaxillary adenitis (Fig. 2). When the gland barriers are passed, the toxin of the streptococcus produces fever and the well-known tired feeling in the legs or actual rheumatic pains.

Fig. 2. Same patient as in Fig. 1, showing tenderness of cervical nodes secondary to chronic sinusitis.

The causes of chronic low-grade fever are numerous, since infection in any part of the body can produce it. Chronic sinusitis probably leads the innumerable causes of chronic low-grade fever, including cases labeled "fever of unknown origin."

Post-infectious hyperthermias[18] are usually the result of concomitant sinus involvement, as after influenza,[19] scarlet fever,[20] measles and other acute infections.

Differential Diagnosis: a. "fever of unknown origin"; b. toxemia from abscessed teeth, gingivitis, pyorrhea, subacute tonsillitis,

recurring otitis media; c. rheumatism and chorea; d. pyelitis and nephritis; e. tuberculosis; f. exercise; g. allergy.

a. *"Fever of Unknown Origin"* is a familiar expression to physicians. These cases are often baffling and may require a complete workup, seeking among other diseases, typhoid fever, undulant fever, malaria, rheumatic fever and hyperthyroidism.

Davison[51] lists many causes of obscure fever in children, "but sinusitis, brucellosis and infectious arthritis are the most likely to be overlooked."

Sohval and Som[52] report 9 cases in which intermittent fever of obscure origin had lasted for weeks and months and various diagnoses had been made, such as rheumatic fever, infectious mononucleosis, typhus and subacute endocarditis. In all these cases the condition was cleared up by careful attention to chronic sinusitis, which in most of them had given little indication of its presence.

b. *Toxemia from Abscessed Teeth, Gingivitis, Pyorrhea, Subacute Tonsillitis, Recurring Otitis Media,* may all cause low-grade fever, usually of minimal degree. Tonsillectomy rarely improves unexplained fever. Kaiser[17] concludes: "Unexplained attacks of fever cannot be shown to have any constant relation to diseased tonsils. Removal of the tonsils offers very little prospect of reducing the frequency of such attacks." Chronic sinusitis in children is the usual source of bacteria which periodically attack the tonsils and may account for fever believed to be caused by infected tonsils.

c. *Rheumatism and Chorea* may commonly cause low-grade fever due to toxins of the streptococcus. In storm areas during the winter and spring months, vague pains, often unrecognized as rheumatic, may be associated with low-grade fever in children.

The prerheumatic state of Coburn, or the rheumatic state,[53] may cause low-grade fever, the symptoms and fever being due to active chronic sinusitis.[54, 55]

When due to the usual focus (the sinuses), the fever of rheumatism may be aborted by use of the head-up position, avoidance of prolonged recumbency, and by the application of hot, wet towels over the face. In acute rheumatic fever such treatment often causes a rapid subsidence of high temperatures and aborts the rheumatic process.[55]

d. *Pyelitis and Nephritis* may be responsible for low-grade fever.

Storms and upper respiratory infection frequently precede febrile episodes.

e. *Tuberculosis* produces either low or high fever during the active process. Fever is present in both the primary and secondary types. In the primary or first-infection type, low-grade fever is present until the primary complex (a triad consisting of tubercle, lymphangitis and lymphadenitis) heals, usually by calcification.

Tuberculosis is frequently diagnosed mistakenly for sinusitis.[56]

Active tuberculosis as a cause of fever is uncommon. In our Chest Clinic tuberculin tests were routine; previous infection with tubercle bacilli, as determined by a Mantoux test, existed in about 20 per cent, but active tuberculosis was a rarity. In contrast to the comparatively small number of positive tuberculin reactors and still fewer cases of active tuberculosis, the incidence of chronic sinusitis was 100 per cent. The diagnosis of sinusitis was made from symptoms, signs, nose and throat consultations and roentgenograms. These children were sent to the clinic mainly for frequent colds and coughs.

f. *Exercise* normally raises the basal metabolic rate and elevates body temperature[48, 57, 58] but to a greater degree in the victim of active focal infection. McKenzie,[28] while stating that fever in chronic sinusitis is usually absent or of low degree, had "several patients in whom temperatures would rise to 103° and 104° F. after a short walk."

Sinusitis aggravates the normal febrile rise after exercise. Charts of most patients with chronic sinusitis at the Pediatric Chest Clinic of New York Post-Graduate Hospital revealed some degree of fever (even though taken between 9:00 A. M. and 11 A. M.) during the season of inclement weather. Rectal temperatures frequently ranged from 100° and 101.5° F.

g. *Allergy* may produce fever. Rowe[59] directs attention to food allergy as one cause of unexplained fever. The most likely explanation of allergic fever is a disturbance in the temperature-regulating center of the brain by a localized or generalized allergic reaction. Proof that fever may be caused by allergy is the dramatic drop in temperature of febrile patients with allergic bronchopneumonia after adrenalin.[60]

16. FATIGUE. Children with sinusitis less commonly exhibit constant fatigue than do adults. However, there are a number

whose parents complain that the child seems lazy or that he is exhausted at the end of the day. Lamont[61] studied 125,00 children in institutions and private practice and concluded: "No hesitation is made in stating that upper respiratory infections account for the greatest amount of fatigue under the heading of morbid fatigue."

Symptoms accompanying fatigue in children with active sinusitis are aches in legs and abdomen, frequent yawning or sighing, spells of irritability, frequent nosebleeds and other "rheumatic" phenomena. Such fatigued children tend to have tachycardia, mitral lesions, precordial pain, frequent colds, sniffing and hacking, circles under the eyes, puffs beside the nose and under the eyes, especially in the morning, anorexia on arising and cervical adenitis. All symptoms improve in hot weather.

Differential Diagnosis: a. carditis; b. rheumatism; c. chorea; d. tuberculosis; e. hypoadrenia; f. allergy; g. leukemia and other blood dyscrasias; h. secondary anemias.

a *Carditis.* Myocarditis is a common cause of fatigue. Because of the considerable heart reserve in children, those who have escaped severe rheumatic fever are not likely to be troubled with cardiac fatigue. However, with increasing age, focal infections tend to damage the myocardium and reduce the cardiac reserve; fatigue is an early symptom of cardiac failure.

b. *Rheumatism* commonly produces fatigue, either as a result of toxemia or by virtue of the accompanying carditis. Since rheumatism is a secondary manifestation, the primary source must be attacked to aid fatigue of this type.

c. *Chorea,* like rheumatism, may be responsible for fatigue. The fatigue of chorea results from muscular hyperactivity and from the effect of toxins on the adrenals and heart.

d. *Tuberculosis* (primary type) in children presents very few early signs or symptoms. Fatigue is one of the most dependable.

e. *Hypoadrenia* is noted in a variety of toxemias, commonly after influenza. Chronic sinusitis may furnish the toxins in some children. Hypoadrenia is seldom recognized, but it may be suspected in children with fatigue, allergy, hypotension, numerous lentigines and moles,[62] and low capillary resistance.[63]

f. *Allergy* is often associated with fatigue. In allergic conditions, such as asthma, fatigue is commonly due to hypoadrenalism.[64]

A number of constantly fatigued children are "born tired" as a result of congenital hypoadrenia.[65]

g. *Leukemia and Other Blood Dyscrasias,* in which anemia is marked, cause chronic fatigue which eventually forces the child to bed.

h. *Secondary Anemias* cause fatigue. The heart and lungs are speeded up to make up for the deficient hemoglobin. Toxin, producing anemia, may also damage the adrenals and heart, thus enhancing fatigue.

17. RECURRENT TONSILLITIS. When attacks occur at frequent intervals, tonsillitis is usually caused by chronic sinusitis.[5]

18. RECURRENT PHARYNGITIS, like recurrent tonsillitis, is usually secondary to chronic sinusitis.[5,33] Tonsillectomy and adenoidectomy do not reduce recurrences of pharyngitis.[5]

19. OTITIS MEDIA is invariably secondary to upper respiratory infections or sinusitis.[66] Recurrent attacks of otitis media are secondary to chronic sinusitis.[67] Chronic otitis media exists only in association with active chronic sinusitis.[33]

Kaiser[68] found no "ear troubles" in the tropics where sinusitis is quiescent. For the same reason, otitis media is seldom seen in hot weather.

Removal of tonsils and adenoids results in greater incidence of otitis media,[69,70] probably due not to loss of tonsils, but to the loss of the protective adenoid.[71,72]

20. MASTOIDITIS is a secondary disease. It follows otitis which in turn is dependent on continued postnasal drainage of sinusitis.[69,73]

21. TINNITUS. Ringing in the ear is seldom a complaint in young children, but is noted in older children. Sinusitis is by far the most constant cause. Hence it is worse with a "cold"[74]. Tinnitus is often associated with a "stopped-up" feeling in the ear and with vertigo on motion. Frequently the tinnitus is unilateral and tends to occur on the side where sinus infection is greater.

Tinnitus occurs in diseases associated with or caused by sinusitis, such as otitis media, pharyngitis and rheumatic fever. Influenza and other infections, which involve the sinuses, may produce tinnitus.[75]

Differential Diagnosis: a. allergy; b. cerumen; c. heart failure.

a. *Allergy.* Following ingestion of food allergens, tinnitus may occur in sensitive subjects. Tinnitus may also accompany hay fever.

Fig. 3. Marked photophobia secondary to sinusitis. As patient appeared upon entering office.

Fig. 4. Showing photophobia after removing his eye-shade.

Fig. 5. Demonstrating marked tenderness, left antrum. Patient had pansinusitis. Note mouth breathing in three photos.

b. *Cerumen* is a rare cause of unilateral tinnitus and deafness in children. Such tinnitus is of sudden onset following a swim or shower and persists until the wax is removed as by syringing the ear.

c. *Heart Failure* in severe rheumatic fever may produce labyrinthine edema and tinnitus.

22. VERTIGO. This is a common symptom in acute and chronic sinusitis. It is rarely found in children under six years of age, but becomes a matter of concern after this age (Fig. 1).

Love[74] believes that posterior sinusitis "has accounted for more cases of vertigo as seen in everyday practice, than all other causes combined."

Rheumatic individuals frequently complain of vertigo when sinusitis is active. It is likely to be noticed upon arising, becoming less troublesome as the day wears on. Any sudden motion of the head may produce vertigo, but it is more severe during a cold or acute sinusitis.

Differential Diagnosis: a. otitis; b. rheumatic fever; c. allergy; d. migraine.

a. *Otitis.* Catarrhal and supurative otitis media, commonly produce vertigo.

b. *Rheumatic Fever* is frequently accompanied by a vertigo of motion.

c. *Allergy* may produce a transient vertigo. Vertigo occurs in angioneurotic edema and in hay fever.

d. *Migraine* causes vertigo on motion.

23. PROGRESSIVE DEAFNESS. This pitiful symptom of sinusitis may start early in childhood. Chronic catarrhal or suppurative otitis media often precedes an awareness of deafness. In the absence of recognized ear infection, every cold tends to make the child more deaf. Such deafness may be mistaken for inattention. Chronic sinusitis is the almost invariable cause of progressive deafness[69, 71, 77, 78]. The deafness which follows influenza, measles and scarlet fever is likely to be caused by the complicating sinusitis.

Differential Diagnosis: a. Congenital deafness may be caused by rubella in the mother during early pregnancy. b. Congenital syphilis may result in deafness; the internal ear is usually attacked between the eighth and twentieth years of life (C. R. Holmes). c. Meningitis produces sudden, not progressive, deafness. d. Traumatic deafness is acute and likely to be unilateral.

(To be concluded in December issue)

NEUTRALIZATION OF COLUMBIA-SK AND YALE-SK VIRUS BY POLIO-CONVALESCENT AND NORMAL HUMAN SERA*

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A considerable body of evidence exists to show that the Lansing type of murine poliomyelitis virus is neutralized by a high percentage of polio-convalescent human sera obtained from patients in unselected series.[1] Neutralization of a similar or even higher order can also be elicited with sera from normal persons.[2] In both cases, the incidence of positive sera increases proportionately with the age of the individuals. These facts are analogous to what has previously been observed in neutralization tests with one given standard strain (Aycock) of simian poliomyelitis virus.[3] While the results are generally interpreted as indicating a specific immune response to the virus following clinical or subclinical exposure, the point remains somewhat problematical because of the failure to demonstrate any significant rise in antibody titer during the course of convalescence, as reported in most of these studies.[4] Serological typing of freshly isolated strains of human poliomyelitis virus has not yet sufficiently progressed to permit any opinion on the frequency of type distribution in various epidemic areas. However, according to data thus far collected, the Lansing-Aycock type has been encountered much less frequently (6 of 27 strains studied) than the immunologically different Brunhilde type (20 of 27 strains studied)[5]. Undoubtedly, further work will provide a better correlation between results obtained from antibody determinations in human sera and results obtained from serological typing of actually infecting strains.

Little information is available concerning the neutralizability of the Col-SK-MM-EMC-Mengo group of viruses by human sera. Early efforts, in 1943, to study this problem for Col.SK virus suggested that among a group of 167 human sera, normal or polio-convalescent, 11 sera apparently neutralized this virus[6]. These results, however, are not strictly comparable to those obtained in other neurotropic virus neutralization tests, since methods and

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criteria differed from those currently employed. In the case of MM virus, Gard and Heller[7] observed the presence of well-marked hemagglutination-inhibitory substances, occasionally with a definite rise in titer during convalescence, in 23 human sera obtained from a group of 171 patients presenting symptoms of central nervous system infection which included various types of poliomyelitis (bulbar, spinal-paralytic, non-paralytic) and encephalo-meningitis. However, none of the positive sera were capable of neutralizing the virus in the mouse test. Against EMC virus, Smadel and Warren[8] reported in 1947 significant antibody levels in 17 of 44 human sera examined, with a second-phase rise in antibody titer in three instances. These sera were from patients hospitalized in Manila (1945-46) with a clinical diagnosis of "Three Day Fever" (aseptic meningitis?, abortive poliomyelitis?). While the diagnosis in these cases is uncertain, the outbreak appears to be one of the several poliomyelitis epidemics described by Paul[9] as occurring among American troops during the war in the Pacific theatre of operations. In a subsequent report by Warren et al.[10] it is stated that, excluding the Manila series, over 300 human sera were examined for neutralizing antibody against EMC virus and only 9 sera were positive. The negative specimens included sera from healthy individuals, from cases of various central nervous system diseases, and from cases with rheumatic fever or idiopathic myocarditis. Of the 9 positive sera, 5 were from patients with a diagnosis of mild or abortive poliomyelitis, 3 from cases diagnosed as mild aseptic meningitis, and 1 from an individual with unexplained upper respiratory infection. With respect to Mengo virus, serum from a patient suffering from accidental infection with this agent neutralized the virus and a significant rise in Mengo antibodies was demonstrated during convalescence. In studies on the distribution of immunity to Mengo virus in Africa, 2 of 143 normal human sera examined contained antibodies in high titer.[11] The available evidence may therefore be summarized by saying that antibodies to the Col.SK-MM-EMC-Mengo group of viruses are rarely found in sera from healthy individuals, whereas a small but variable percentage of positive specimens may be obtained from cases diagnosed as aseptic meningitis, a mild, abortive poliomyelitis, or as polio-encephalomyelitis.

Materials and Methods. The present paper deals with a study

of the neutralization of Col.SK virus and of Y-SK virus by: (a) polio-convalescent human sera, (b) normal human sera, (c) normal human gamma globulin. The polio-convalescent sera, for the greater part, were obtained from patients hospitalized at the Kenny Institute of the Jersey City Medical Center. One group of 36 sera came from patients stricken in 1948, while another group of 91 sera was obtained from patients admitted during the epidemic of 1949 involving the Greater Metropolitan Area. Practically all of the 1948 sera were from patients with moderately severe or severe paralytic involvement and included children as well as adults. The 1949 series comprised sera from children diagnosed as paralytic and non-paralytic poliomyelitis. The diagnosis was based on the commonly accepted clinical and laboratory criteria, with a range in symptoms as is usually observed in the course of a major epidemic. All of the above sera, with few exceptions, were collected during the acute stage of the disease, i.e., within the first 2 or 3 weeks after the onset of clinical signs. A small group of 5 sera was obtained early in 1949 from Mexican children, diagnosed as paralytic or non-paralytic poliomyelitis, who had contracted the disease in the summer of 1948 during a sharp outbreak of poliomyelitis in Saltillo, Mexico. The authenticity of this epidemic was reasonably established through correspondence with the local Health Department and the attending physician. The "normal" sera consisted of a group of 39 random specimens obtained from medical students at Columbia Medical School and of a small group of 12 sera from healthy individuals, aged 14, living near New Haven, Conn. There is also included, for purpose of control, a group of 20 sera from healthy pregnant women, living in New York City, who were bled at various stages of pregnancy. The "normal" human gamma globulin was from one batch, prepared for the American Red Cross, and was provided through the kindness of the New York City Health Department.

Col.SK Virus Neutralization Test. The technique used in these tests consisted of mixing 0.5 cc. of undiluted serum with 0.5 cc. of serial ten-fold virus dilutions (10^{-4} to 10^{-9}), holding the mixtures for 1 hour at 37°C. and overnight in the icebox, and injecting aliquot amounts of each virus-serum mixture intraperitoneally into groups of 4 young (10-12 gm.) Swiss albino mice, each mouse receiving a volume of 0.2 cc. The animals were observed over a

Table I

Neutralization of Col.SK and Y-SK Virus by Polio-convalescent Human Sera

Year	Locality	Col-SK Virus Neutralization Index					Y-SK Virus Neutralization		
		Number	Negative		Positive		Number	Negative	Positive
			0-9	10-99	100-999	1000+			
1948	Greater New York	36	16*	10	7**	3***	9	0	9
1949	" " "	91	59	15	12	5	84	42	42
1948	Saltillo, Mexico	5	4	0	0	1	5	4	1
			79	25	19	9			
Total		132	104(79%)		28 (21%)		98	46(47%)	52(53%)

* This group includes two sera from paralyzed pregnant women.
** This group includes one serum from a paralyzed pregnant woman.
*** This group includes two sera from paralyzed pregnant women.

period of 10 days. All of the sera were unheated, but most of them had been stored for some time in the icebox. In a few instances, tests were repeated with the same specimens after they had been heated for one-half hour at 56° C. Judging from our limited experience, this procedure did not seem to have any decisive effect on the results. Tests were usually run with groups of from 5 to 15 sera, each experiment being controlled by the addition of samples of normal monkey serum (M. rhesus or M. cynomolgus). To ensure maximum and uniform viral potency, the virus was always harvested freshly from paralyzed passage mice, no less than 3 brains being pooled to prepare the suspension. Neutralization indices were computed by comparison of the LD_{50} values of the control serum with the LD_{50} values of the test serum. By running test and control serum up to true endpoints of viral potency, little or no difficulty was experienced in arriving at a correct statistical evaluation of the neutralizing activity of a given specimen. Sera which failed to neutralize at least 100 LD_{50} of virus were considered negative, whereas those neutralizing between 100 and 1,000, or more, LD_{50} of virus were listed as positive.

Y-SK Virus Neutralization Tests. These tests were performed by mixing 0.3 cc. of undiluted serum with 0.3 cc. of a 10^{-1} virus suspension, holding the mixture 1 hour at 37° C. and overnight in the icebox, and injecting aliquot amounts of the virus-serum mixture intracerebrally into groups of 8 young (10 gm.) Swiss albino mice, each mouse receiving a volume of 0.03 cc. A normal monkey serum control accompanied each experiment. The animals were observed over a period of 30 days. The virus was harvested from the brains and cords of freshly paralyzed mice and showed an LD_{50} of 10^{-8} in repeated intracerebral titrations. A serum was considered positive if 50 per cent or more of the mice survived, whereas at least 87.5 per cent of the control mice died with paralysis. While border-line results, which necessitated repetition, occurred occasionally, in most instances there was no difficulty in deciding whether a positive specimen had clearly inactivated at least 100 LD_{50} of virus.

Results. The results obtained in these tests have been brought together in Tables I, II, III and IV.

It appears from Table I that of a total of 132 polio-convalescent human sera tested, 104 (79 per cent) were negative, whereas 28

(21 per cent) contained significant antibody levels against Col.SK virus. The corresponding figures for a total of 98 sera tested against Y-SK virus were 46 (47 per cent) negative and 52 (53 per cent) positive. Therefore, the frequency of neutralization of Y-SK virus exceeded that of Col.SK virus by a ratio greater than 1:2. When a comparison is made for Col.SK and Y-SK virus neutralization by individual serum samples (Table II), it

Table II

Y-SK Virus Neutralization by Col.SK Positive and Col.SK Negative Polio-Convalescent Human Sera

Sera	Number	Y-SK Virus Neutralization	
		Positive	Negative
Col.SK positive	19	12	7
Col.SK negative	79	40	39

will be noted that a majority of the Col.SK-positive sera were also positive for Y-SK virus; on the other hand, about one-half of the Col.SK-negative sera also possessed neutralizing capacity for Y-SK virus.

The data concerning the neutralization of Col.SK and Y-SK virus by "normal" human sera are given in Table III. It will be seen that among a total of 71 sera examined 60 (84 per cent) failed to neutralize and 11 (16 per cent) did neutralize Col.SK virus. Among 14 sera of that group tested against Y-SK virus 4 (29 per cent) were negative and 10 (71 per cent) were positive for that virus. Therefore, the frequency of Y-SK virus neutralization exceeded that of Col.SK neutralization by a ratio greater than 1:6. In interpreting the overall figures for Col.SK virus neutralization allowance must be made for the fact that the series of 39 sera from healthy medical students included sera from two individuals with a definite history of abortive or paralytic poliomyelitis, both of which were markedly positive. It should also be mentioned that 5 positive reactions were found in a group of sera of 20 healthy pregnant women. That pregnancy sera from

Table III

Neutralization of Col. SK and Y-SK virus by "Normal" Human Sera

Year	Locality	Individuals	Col.SK Virus Neutralization Index					Y-SK Virus Neutralization		
			Number	Negative		Positive		Number	Negative	Positive
				0	10-99	100-999	1000+			
1948	New York, N.Y.	Medical students	39	30	5	2	2*	2	0	2*
1949	New York, N.Y.	Healthy pregnant women	20	10	5	4	1			
1949	Ansonia, Conn.	Healthy adolescents	12	10	0	1	1	12	4	8
Total			71	50	10	7	4	14	4(29%)	10(71%)
				60(84%)		11(16%)				

* This group includes one student with a history of abortive poliomyelitis contracted in 1948 in Saltillo, Mexico and another student with a history of paralytic poliomyelitis contracted in 1946 in New London, Conn.

man and certain animals may yield an unusually high percentage of "non-specific" neutralization has previously been observed in tests with simian or murine poliomyelitis virus.[12, 13, 14] The phenomenon is unexplained, particularly since the high level of serological activity stands in strange contrast with the greater risk for poliomyelitic infection as recorded for both the human and experimental disease.[15, 16]

The results obtained with "normal" human gamma globulin are given in Table IV. It appears that this preparation, undiluted and in high dilutions, was capable of bringing about marked neutralization of both Col.SK and Y-SK virus. The data are in agreement with those recently reported by Bodian[17] for the inactivation of several strains of simian poliomyelitis virus. However, as far as the specificity of the Col.SK virus inactivation is concerned, caution is necessary in interpreting the reactions obtained with the two highest dilutions of gamma globulin, since normal monkey serum, in corresponding dilutions, also showed some progressive inhibitory effect on the virus. The possibility of any chemical inactivation by means of the preservative (sodium ethylmercurithiosalicylate 1:10,000) can be excluded, since normal monkey serum, similarly preserved, failed to exhibit any antiviral effects. On the other hand, it is known that virus, in high dilutions, is markedly less stable in saline or in distilled water than in a well-buffered serum medium.

DISCUSSION

The data reported in this paper show that approximately one-fifth of human sera obtained from patients during the acute stage of paralytic or non-paralytic poliomyelitis have significant antibody levels for Col.SK virus.* Since there was no opportunity for following the serum reaction through convalescence, it is impossible to assert the specific nature of the phenomenon. Comparative tests with Y-SK virus show that this virus is neutralized by slightly more than half of the polio-convalescent sera from patients in the same series. Thus, the percentage of Y-SK positive sera is considerably higher than that of Col.SK positive sera. The precise significance of these neutralization phenomena is difficult to assess. On the one hand, the ability to neutralize Y-SK virus seems to be

*In two small series of acute cases diagnosed as aseptic meningitis of unknown etiology, 4 from New York City (1947) and 8 from St. Gallen, Switzerland (1948-49)—2 Col.SK positive sera were found, one in each series.

Table IV

Neutralization of Col.SK and Y-SK Virus by "Normal" Human Gamma Globulin

Serum	Col.SK Virus Dilutions 10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	10^{-7}	10^{-8}	10^{-9}	Y-SK Virus Dilution 10^{-1}
Gamma globulin*									
Undiluted	4/4	4/4	1/4	0/4					2/8
1:10	3/4	3/4	0/4	0/4					1/8
1:100	4/4	4/4	1/4	1/4					1/8
1:1000	4/4	4/4	1/4	0/4					
Normal monkey serum									
Undiluted	4/4	4/4	4/4	4/4	4/4	4/4	3/4	2/4	8/8
1:10	4/4	4/4	4/4	4/4					7/8
1:100	4/4	4/4	4/4	3/4					7/8
1:1000	4/4	4/4	3/4	2/4					

Numerator = Number of mice paralyzed.
Denominator = Number of mice injected.

* Lot No. C4569 (160 mgm. gamma globulin per 1.0 cc.).

an almost universal property of normal human sera in geographically unselected series, once the donors have passed the age of childhood. On the other hand, the difference between the frequency of neutralization of Col.SK virus given by polio-convalescent and by normal sera does not appear highly significant in this work, although it is true that marked neutralization (index 1000 plus) was rarely observed with specimens from healthy individuals in whom a previous attack of poliomyelitis, abortive or paralytic, could be excluded. The fact that normal human gamma globulin seems to be equally effective in its neutralizing action on both Col.SK and Y-SK virus suggests a possible operation of the same pathognomonic principle in concentrated form.

If one accepts the conventional standards of epidemiological interpretation, the observations would indicate that the Col.SK group of viruses occurs as a human-pathogenic entity in urban populations of the Northeastern United States, producing poliomyelitis or a poliomyelitis-like clinical picture in the wake of a typical epidemic, although at a much lower rate of frequency than can be postulated from similar evidence for the Lansing-Y-SK group of viruses. Of special interest seems the fact that Col.SK-MM-EMC-Mengo antibodies in human sera have been encountered not only in the United States but also in the Philippines, Mexico and Africa. These serological findings are paralleled by the topographic isolations of this type of virus in the Northeastern United States (Col.SK virus, MM virus, New England states) and also in subtropical (EMC virus, Florida) and tropical (Mengo virus, Uganda) areas of the world. Therefore, a thought, first implied by Lépine,[18] namely, that the Col.SK group of viruses may not be native to the United States but may have been imported through travel or other means of communication, deserves serious consideration.

SUMMARY

A series of 132 sera from patients diagnosed as paralytic or nonparalytic poliomyelitis, most of which were obtained during the acute or subacute stage of the disease, were examined for neutralization of Col.SK and Y-SK virus. Significant antibody levels were observed for Col.SK virus in approximately one-fifth (21 per cent) and for Y-SK virus in approximately one-half (53 per cent) of

these sera. A series of 71 "normal" human sera was examined for neutralization of Col. SK virus. Eleven positive reactions were observed in this group. Two of the positive sera were obtained from individuals with a definite history of abortive or paralytic poliomyelitis and 5 from healthy pregnant women. A batch of "normal" human gamma globulin was markedly virucidal for both Col.SK and Y-SK virus. The significance of these neutralization phenomena is discussed.

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REFERENCES

1a. Hanford, C. G. and Bronfenbrenner, J.: Serum Protection Tests with the Lansing Strain of Murine Poliomyelitis Virus. Proc. Soc. Exper. Biol. & Med., 47, 211-215, 1941.
b. Hammon, W. McD. and Izumi, E. M.: Poliomyelitis Mouse Neutralization Tests Applied to Acute and Convalescent Sera. Proc. Soc. Exper. Biol. & Med., 49, 242-245, 1942.
c. Turner, T. B. and Young, L. E.: Mouse-adapted Lansing Strain of Poliomyelitis Virus; Study of Neutralizing Antibodies in Acute and Convalescent Serum of Poliomyelitis Patients. Am. J. Hyg., 37, 67-79, 1943.
d. Hammon, W.; Mack, W. N. and Reeves, W. C.: The Significance of Protection Tests with the Serum of Man and Other Animals against the Lansing Strain of Poliomyelitis Virus. J. Immunol., 57, 285-299, 1947.
e. Pait, C. F.; Kessel, J. F. and Grossman, P.: The Neutralization of the Mouse-Adapted Poliomyelitis Virus by the Sera of Patients, Family Contacts, and Normal Children in Los Angeles. Am. J. Hyg., 47, 335-344, 1948.
2a. Haas, V. H. and Armstrong, C.: Immunity to the Lansing Strain of Poliomyelitis as Revealed by the Protection Test in White Mice. Publ. Health Rep., 55, 1061-1068, 1940.
b. Turner, T. B.; Young, L. E. and Maxwell, E. S.: The Mouse-adapted Lansing Strain of Poliomyelitis Virus; Neutralizing Antibodies in the Serum of Healthy Children. Am. J. Hyg., 42, 119-127, 1945.
c. Bell, E. J.: The Relationship between the Antipoliomyelitic Properties of Human Nasopharyngeal Secretions and Blood Serum. Am. J. Hyg., 47, 351-369, 1948.
3a. Jungeblut, C. W. and Smith, L. W.: Blood Grouping in Poliomyelitis. Its Relationship to Susceptibility and the Neutralizing Property of Convalescent Sera. J. Immunol., 23, 35-47, 1942.
b. Jungeblut, C. W.: The Power of Normal Human Sera to Inactivate the Virus of Poliomyelitis in its Relationship to Blood Grouping and Exposure. J. Immunol. 24, 157-172, 1943.
4. Brown, G. C. and Francis, T.: The Neutralization of the Mouse-adapted Lansing Strain of Poliomyelitis Virus by the Serum of Patients and Contacts. J. Immunol., 57, 1-10, 1947.
5. Kessel, J. F. and Pait, C. F.: Immunologic Groups of Poliomyelitis Viruses. Am. J. Hyg., 51, 76-84, 1950.
6. Jungeblut, C. W. and Seligmann, E.: Neutralization of SK Murine Poliomyelitis Virus and of Theiler's Virus of Mouse Encephalomyelitis by Human Sera. Am. J. Pub. Health, 33, 1326-1332, 1943.
7. Gard, S. and Heller, L.: Hemagglutination par le Virus Col-MM. Proc. Third International European Poliomyelitis Conference Amsterdam, 1950.
8. Smadel, J. E. and Warren, J.: The Virus of Encephalomyocarditis and Its Apparent Causation of Disease in Man. J. Clin. Investigation, 26, 1197, 1947.
9. Paul, J. R.: Poliomyelitis Attack Rates in American Troops, 1940-1948. Am. J. Hyg., 50, 57-62, 1949.
10. Warren, J.; Smadel, J. E. and Russ, S. B.: The Family Relationship of Encephalomyocarditis, Col. SK, MM, and Mengo Encephalomyelitis Viruses. J. Immunol., 62, 387-398, 1949.
11. Dick, G. W. A.: The Relationship of Mengo Encephalomyelitis, Encephalomyocarditis, Col. SK, and MM Viruses. J. Immunol., 62, 375-386, 1949.
12. Jungeblut, C. W. and Engle, E. T.: The Influence of Pregnancy and of Menstruation on the Power of Normal Human Sera to Inactivate Poliomyelitis Virus. J. Immunol., 24, 267-272, 1933.

13. Jungeblut, C. W.: Further Observations of the Poliocidal Property of Pregnant Mare Serum. Proc. Soc. Exp. Biol. & Med., 33, 137-141, 1935.
14. Sabin, A. B.: Antipoliomyelitic Substance in the Milk of Human Beings and Certain Cows. Presented at the Meeting of the Am. Pediat. Soc., French Lick, Ind., May 9, 1950.
15. Knox, A. W.: Influence of Pregnancy in Mice on the Course of Infection with Murine Poliomyelitis Virus. Proc. Soc. Exp. Biol. & Med., 73, 520-523, 1950.
16. Byrd, C. L.: The Influence of Infection with Lansing Strain of Poliomyelitis Virus on Pregnant Mice. J. Neuropath. & Exp. Neurol., 9, 202-203, 1950.
17. Bodian, D.: Neutralization of Three Immunological Types of Poliomyelitis Virus by Human Gamma Globulin. Proc. Soc. Exp. Biol. & Med., 72, 259-261, 1949.
18. Lepine, P.: L'état actuel de l'immunologie de la poliomyélite. Proc. Second International European Poliomyelitis Conference, Paris, pp. 167-174, 1949.

BONE CHANGES IN LEUKEMIA. (Revista Chilena de Pediatria, Santiago, 21:289, July 1950). Hasbun and Eberhard report nine cases of acute lymphatic leukemia in children in whom the diagnosis was facilitated by periodic roentgen examination of the bones. Bone lesions visible in the roentgenograms are frequent in acute lymphatic leukemia of children. Lesions in eight cases were located in the distal metaphysis of the femur and in the distal ends of the radius and the ulna in one case. The roentgen picture was of the osteolytic type in five cases and of the osteochondrotrous subperiosteal and osteosclerotic types in the other four cases. Osteomyelitis is differentiated from acute lymphatic leukemia, in patients who present bone lesions and local pain, by examination of the blood and the bone marrow obtained by sternal puncture.—*Journal A.M.A.*

EFFICACY OF ACETARSONE IN CONGENITAL SYPHILIS. (Acta Paediatrica, Stockholm, 39:122, 1950). Nyhus reports on 34 infants treated with acetarsone for congenital syphilis in an Oslo hospital. Of these patients, 30 came for follow-up examinations from two to 18 years after termination of treatment. One had positive seroreactions and positive Wassermann reaction in the spinal fluid. The remaining patients were healthy, except for two who had had traumatic brain injury at birth, and had spastic paraplegia of the lower extremities. Four of 23 patients had Hutchinson teeth. There were no skull changes. The intelligence quotient tests revealed that 16 patients were normal, eight were backward, five were feebleminded and one an idiot. Mental defects were demonstrated in the majority of the parents of the retarded children. Poor inheritance, therefore, may have been the cause of the reduced intelligence of the children with congenital syphilis.—*Journal A.M.A.*

PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

THE TONSIL AS A PORTAL OF MICROBIC AND TOXIC INVASION*

A. JACOBI, M.D.
New York.

You have been good enough to re-elect me to the position I occupied during the early part of the existence of this Society. The honor, for which I thank you from the innermost of my heart, was surely unexpected; for a re-election under these circumstances is unusual. Let me now, however, that I have been the recepient a second time of this great distinction, suggest to you the possibility of abolishing the old custom of never according a re-election to a former incumbent. There may be reasons for not changing it, but I can imagine that the Society may not forever bind itself to persist in annual changes. The desire to become the presiding officer of this distinguished body is justifiable and natural, but it may be in its occasional interest to reappoint a former officer.

My present remarks should not be considered in the light of a formal address. Nothing I could present to you satisfies my wish to serve you; but the exigencies of the past weeks have prevented me from coming before you with an essay worthy of the occasion. Still, it occurred to me that you would be satisfied with the consideration of a problem which appears to become less soluble the more copious its literature has grown. What I allude to is the rôle the tonsil plays in the absorption of bacteria or toxins. Clinical observations on that subject are very numerous, and deserve the same credit due to every accurately observed fact; but will rarely be numerous enough to decide the exclusive or partial port of entry of a poison into the circulation. For we are seldom in a position to separate the tonsil from its neighborhood during the

*Presidential address at the Eighteenth Annual Meeting of the American Pediatric Society, held at Atlantic City, N. J., May 30, 1906.
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acute invasion or the rapid progress of a microbic or toxic poison. Altogether, I mean to approach the subject as well from an anatomical point of view as from that of clinical experience.

At the head of what I have to say I place observations I have made many hundreds of times, formulated in papers and books repeatedly these forty and more years, and which have been confirmed by the observations of others. Cases of membranous throat diseases behave differently according to their location. What we called diphtheria in 1858 and twenty-five years afterwards and at present either diphtheria, or pseudodiptheria, or coccus invasion, or what not, behaves alike in its relation to the lymph system and especially to the lymph bodies of the neighborhood. The observations are easy, because in these affections there is a visible result of the invasions in the shape of membranous tufts or layers, and the invasion itself can be traced to an almost always definite day followed by a brief incubation, contrary to what we know of the invasion of tuberculosis. Now, whenever the membrane is limited to the tonsil there is very little or no glandular swelling in the neighborhood. On the other hand, if a membrane extends from the tonsil to its neighborhood, or starts at a distance from the tonsil, neighboring lymph bodies swell at once. Again, the treatment of this neighborhood shows its effect almost immediately on the swelled glands. That is mostly evident when the seat of the membrane is anywhere in the posterior nares which excel by an immense network of lymphatics. On the other hand, when it covers the vocal cords and Morgagni's fossa, both of which have only a scanty network of lymphatics, there is no adenitis nor any constitutional symptoms. Indeed, it has been well-known these thirty years that an uncomplicated case of laryngeal diphtheria, so-called pseudomembranous croup, is not attended with either glandular swelling or fever. These clinical observations have stood the test of time and must be reckoned with. If there were no rational explanation at present we should have to wait for it, for it would not be the first time for the explanation to lag behind the observation and frequent confirmation of a fact.

For an explanation we shall have to look, if anywhere, to the anatomy of the parts. If a laryngeal pseudomembrane causes no glandular swelling and no fever, and we recognize the cause of this fact in the scantiness of the lymphatic network, we turn to the

tonsil with the attempt at ascertaining whether the isolation of the morbid product on the surface or in the interior of the tonsil depends on a similar anatomical condition.

From my treatise of diphtheria published in 1880 I beg to quote the following lines:

"The tonsils are conglomerations of an indefinite number of glandular bodies, each of which has a thick capsule which is of irregular shape, and consists of connective tissue lined by mucous membrane and pavement epithelium. The connective tissue contains a number of closed follicles, each inclosing numerous lymph-corpuscles. These follicles have been considered identical with, or analogous to, the lymphatic glands; this assumption is purely problematical, since it has not been possible, thus far, to verify the existence of afferent or efferent ducts of their own. The practical deduction from this is, that the tonsils have little or no connection with the lymphatic system. The number of blood-vessels in the normal tonsil is not large, and it becomes greatly diminished when that organ has been the seat of repeated chronic inflammations. It is in these very cases of chronic inflammation and enlargement of the tonsils, with considerable hypertrophy of the connective tissue, that, for instance, diphtheric attacks are most frequently observed, especially, of course, when a fresh irritation has given rise to inflammation and an edematous enlargement."

This statement of our knowledge of 1880 requires, as you will see, in the light of later anatomical research, some modification; one of the tonsil's functions is surely that of either preparing or storing leukocytes. In the embryonic life the thymus is the first to perform that function. Does its rôle pass to the tonsil in the born child? We should hesitate to accept that without caution, for the thymus continues to grow absolutely for several years after birth. Or are both thymus and tonsil replaced by solitary follicles and the adenoid tissue of the appendix in later life? Here again is a reason to pause. For the appendix grows smaller with increasing years, relatively, aye even absolutely. The tonsil is a type of conglomerated follicular glands, ten to twenty according to Koelliker, eight to fifteen, according to Hodenpyl. It is perforated by crypts which unit in two or three long and deep pockets or form in rare cases a deep fissure (similar to what, according to Schmidt, is often found in certain animals).

The external adherent deep surface is covered by a fibrous capsule and outside it by the amygdalo-glossal, upper constrictor, and stylopharyngeal muscles. This fibrous capsule is of various thickness; sometimes so disposed, according to Hodenpyl, as to send along the tonsillar bloodvessels a network of fibrous tissue which prevents them from ready contraction after having been cut. That occurrence furnishes the explanation of the occasional hemorrhages, after resections, from the tonsillar stump, though the anterior palatine artery be not touched at all. But thick or thin, coming from the fibrous membrane of the pharynx, the fibrous capsule is firm and solid. That is why abscesses of the tonsil do not open into the maxillopharyngeal space. From it, like Hodenpyl's periarterial processes, it sends off connective tissue into and between the folds of the mucosa.

(Our textbooks are not particularly accurate. F. H. Gerrish [a textbook of anatomy by American authors, 1902, p. 730] has only this to say, that the tonsil's "external surface is attached to the upper constrictor by areolar tissue." The textbook of anatomy, by D. J. Cunningham, New York, 1905, p. 1036, expresses itself as follows: "The outer or attached surface of the tonsil is enclosed in a distinct fibrous capsule connected with the pharyngeal aponeurosis, outside which lie the superior constrictor of the pharynx and the internal pterygoid muscles." Gray's anatomy of 1897, p. 935—older than most references quoted by me—when speaking of the lymph circulation of the tonsils, says: "Surrounding each follicle is a close plexus of lymphatic vessels. From these plexuses the lymphatic vessels pass to the deep cervical glands in the upper part of the neck, which frequently become enlarged in affections of these organs." Cunningham says only: "The lymphatics are extremely numerous and pass down to join some of the submaxillary lymphatic glands near the angle of the jaw." Retterer, Hodenpyl, Labbé and Poirier are not quoted.)

It should be added, that it also contains in its tissue thick lymphatic trunks, bloodvessels and, according to Koelliker, contracting muscular fibres emanating from the superior constrictor. Whether these lymphatic trunks can ever be active depends on the condition of the lymph circulation within the tonsil itself.

It is reasonable to conclude that as long as a tonsil is normal, not inflamed, either acutely or chronically, it will behave more or

less like a normal tonsil treated on the laboratory table. That is, almost like injection material, living invading material may enter the lymph circulation, or the blood circulation, provided there is a break in a wall, but not with the same facility as injection material forced in. A surface lesion must always be supposed to exist when a living germ or a toxin is to find access. If that were not so, no human or inferior animal could exist under the clouds of microbes and toxins surrounding us. There is only one exception. Stoehr has shown small gaps between the normal epithelia of the surface of the tonsil. It looks rational, therefore, to admit that when there is merely a surface lesion, though ever so slight, there may be an invasion into the tonsil. When, however, the vessels are exposed to pressure by newly formed cells or tissue, there is no invasion, certainly not beyond the tonsil itself, no ganglionic swelling, no toxic poisoning.

It is even rational to believe that now and then, when tonsils, or, what is more common, a single follicle, becomes inflamed, the very venous obstruction will exert the bactericidal influence of the stagnating blood serum.

The lymph vessels of the pharynx come from two sources, from the mucous membrane and from the muscles. The muscular network is of little importance. Even Sappey did not inject it except in cattle and the horse. The mucous network is immediately under the epithelium of the surface; and is mostly developed in the pharyngolaryngeal grooves and on the posterior wall of the larynx.

(I mean to add here, not on the vocal cords; that explains, as I have done these more than thirty years, the absence of constitutional symptoms in purely laryngeal diphtheria; that is, uncomplicated "membranous croup.")

On the level of the palatine tonsil—that is, not on the tonsil itself—the mucous network of the lymph current presents an unusual richness and its walls are very thin. Near the esophagus there are few lymph vessels.

Collecting trunks there are three: First, upper; second, middle; third, lower. The first and third do not concern us today. The second comes not so much from the tonsils as from the mucous membrane of the adjacent parts. They perforate the muscular

tunic just above the big horn of the hyoid bone. Its ganglia are just below the posterior belly of the digastric muscle.

The second volume, p. 1297, of Poirier and Charpy's Anatomy, treating of the tonsil, says nothing of the lymph vessels and its efferent trunks of the tonsils, but the fourth volume does. I refer to p. 92. The lymph vessels of the tonsils originate, first, in the cul-de-sac descending from the surface of the crypts; second, from the ringform nets situated around the follicles; third, from the interfollicular tissue. They all form a network which finally, according to Poirier, but not to many others, passes into the fibrous capsule, where they swell into long trunks containing valves and ganglionic enlargements and at last, together with the lymph ducts of the base of the tongue, end in the submaxillary ganglia near the angle of the jaw and near the hyoid bone. *There are, however* (Labbé), *no lymphatic sinuses around the tonsil,* such as you see around ganglia in other parts of the body.

Now comes a very important statement: Retterer (1886) concluded from his injections of gelatin and silver nitrate, that the lymph net occupies the whole follicular mass of the tonsils, and constitutes in these organs a system of closed canals which *do not open into* the connective reticulum either by open stomata or by extensive outrunners. This is confirmed by Hodenpyl, though denied by other observers.

A. Most (*Arch. f. Anat. u Entw. gesch.*, 1901, p. 86), one of the latest investigators, had the following experience: While injecting the lymph vessels of the lateral pharyngeal wall, the effect was governed by the exact location. "When an injection was made near the pharyngeal tube orifice, it would run in both directions, both backwards and forwards; when in the region of the tonsil, the injected material would run off to the anterior parts of the fauces only." This suggests limited or absent absorption posteriorly. Thus, even near the tonsil, not to speak of the tonsil itself, there is less lymph circulation than posteriorly. "The lymph vessels of the tonsils and of the neighboring mucous membranes, and of the anterior and posterior palatine arches, gather in three or five efferent trunks. They finally arrive at glands which lie laterally of the jugular vein and near or below the lateral belly of the digastric muscle. One lymph body is located in the angle formed by the anterior facial and the internal jugular." Thus,

under very favorable circumstances, there must be a possibility of the contents of the lymph circulation getting away from the tonsil.

One of the very latest writers, perhaps the latest, is George Bacon Wood. He published an essay on the lymphatic drainage of the faucial tonsils in the *American Journal of the Medical Sciences*, August 1905. Wishing to do justice to my subject, I quote from him largely, for it must be supposed that before writing a mongraphic essay he made himself perfectly acquainted with the literature of the subject. "It has been proven," he says, "by several very thorough and capable investigators that foreign bodies in the crypts can pass through the epithelium into the interfollicular tissue. This interfollicular tissue consists of a fine connective tissue reticulum interspersed with numerous lymphoid cells. These pass into the lymph spaces which terminate in the trabeculæ of the tonsil and which in their turn empty into the efferent lymphatics of the tonsil." Thus the author thinks a current is established into which the said foreign bodies are introduced. He also reports that he forced injection material by gentle massage (p. 220) into the efferent lymph ducts and a few of the lymph bodies of the neck and suggests that bacteria may get into the body by their own locomotion or by their growth. And he adds verbally: "I have not been able to find any reliable published data concerning the glands that receive the efferent lymphatics of the tonsils." And on p. 127 he has what follows: "I understand thoroughly that in advancing this idea, I am open to criticism for theorizing about a scientific subject. It seems to me, however, that the above is a probable explanation of the mechanism of tonsillar absorption and helps to substantiate the theory that the faucial tonsil is more important as a source of infection than is the lymphoid tissue on the lateral folds and posterior wall of the pharynx."

In all of this I think he is open to exactly the criticism he means to disarm. What he should set out to demonstrate he has not demonstrated.

One of the glands, under the sternocleidomastoid where it is crossed by the digastric muscle, he claims as tonsillar. His injections were not equally successful. It receives lymph from the lymph bodies of the throat also. Finally, our author says (p. 224): "The most important infections of the cervical lymphatics originate

through the tonsil, and because of the importance of the tonsil in the origin of the infections, I feel that the term tonsillar is a most appropriate one." He takes things too easy. What he sets out to prove he simply postulates. He takes the theory of tonsillar invasion for granted, wisely concludes there must be a sufficient number and calibre of afferent and efferent vessels, and courageously postulates as an anatomical fact what he proposes as a theory.

A number of facts should be considered in connection with the structure and the absorbing and transmitting power of the tonsil. Its surface epithelium is, according to Stoehr, not uniform, and may admit foreign material even without a lesion. Thus an invasion into the normal tonsil is possible.

A catarrh, with destruction of epithelium, may add to that possibility.

The lymph current near the tonsil is less active than that of the pharynx at some distance. There are, moreover (Labbé), no lymphatic sinuses round the tonsil.

There is a system of closed canals *in the follicles* which *do not open* into the connective reticulum. This observation of Retterer is confirmed by Hodenpyl.

The external deep surface of the tonsil is covered by a firm fibrous capsule. Still, according to many, there is a lymph communication between the tonsil and at least one gland situated near and below the crossing of the sternocleidomastoid and digastric muscles.

Exposure, and many diseases, change the surface and the structure of the tonsil.

Every new inflammation changes them. New cell infiltration and cicatricial tissue renders absorption less possible. Blood and lymph vessels are compressed and undergo atrophy. That is why in advanced life the tonsil gets harder and smaller, and infections become less. No tonsil remains long in its original condition; and the same deleterious influences will no longer prove effective.

Laboratory injections into the normal tonsillar structure are made under pressure, and prove nothing, or very little, for the unembarrassed organ when *in situ*, and surely not under pathological conditions. Thus, while the normal infantile tonsil which has not suffered from previous exposure or disease may or must be believed to permit *some* invasion into the tonsillar structure,

and sometimes even beyond it, microbic invasion through the tonsil is not predominant over that which takes place through the lymph apparatus of the pharynx.

That agrees perfectly with the clinical observation of local toxic affections of the oral cavity, according to which membranous affections limited to the tonsil cause no, or little, adenitis or constitutional symptoms.

OTITIS MEDIA IN NEWBORN INFANTS. (Geburtshilfe und Frauenheilkunde, Stuttgart, 10:254, April 1950). Mucus and amniotic fluid, which are always present in the nasopharynx of a newborn infant, may enter the middle ear by aspiration through the eustachian tube and cause a foreign body otitis. This otitis may provide a favorable medium for the development of a purulent otitis media. Prognosis is favorable in the absence of complications. Occult mastoiditis associated with toxic nutritional disturbances is characterized by the absence of mastoid symptoms and by few signs. Severe vomiting, rapid loss of weight and refractory alimentary disturbances are typical. The onset of occult mastoiditis frequently coincides with a period in which latent otitis media or the residua of foreign body otitis are still present, thus providing a medium for the occult mastoiditis. The mortality rate was high in the reported cases.—*Journal A.M.A.*

HEREDITARY FACTORS IN PEPTIC ULCER. (Annals of Eugenics, London, 15:135, March 1950). Doll and Buch compared the incidence of peptic ulcer in the living sibs and parents of 300 ulcer patients with the incidence of peptic ulcer in a control population. They observed an excess of ulcer in the brothers, sisters and fathers of the propositi. The authors conclude that hereditary factors are of importance in the development of peptic ulcer. Evidence was obtained that familial tendencies were more prominent in duodenal ulcer patients and in those with early onset, but the differences were not statistically significant. A strong tendency was observed for sibs to have ulcers in the same site, irrespective of whether the site was duodenal or gastric.—*Journal A.M.A.*

BOOK REVIEWS

PEDIATRIC X-RAY DIAGNOSIS. By John Caffey, M.D. Cloth. Pp. 862. Illustrated. Price $22.50. Chicago: The Year Book Publishers, Inc., 1950.

This is the second edition of a work which first appeared in 1945. In this short span of time it has established itself as a standard textbook in its field. The x-ray reproductions, both touched and untouched, are clear and true and make excellent teaching material. This book should be used as a supplement to any good book on pediatrics and is an excellent source of reference to both the general practitioner and to the roentgenologist who does not see too many children. I would like to quote from the preface to the first edition: "He who would comprehend Röntgen's pallid shades needs always to know well the solid matrix whence they spring. The physician needs to know intimately each living patient through whom racing black light darts, flashes hidden depths to reveal them in a glowing mirage of thin images, each cast delicately in its own halo, but all veiled and blended endlessly."

MICHAEL A. BRESCIA, M.D.

THE PHYSICIAN EXAMINES THE BIBLE. By C. Raimer Smith, M.D. Cloth. Pp. 394. Price $4.25. New York: Philosophical Library, 1950.

This book shows that the author has read the Bible from which he has culled many references to medical and allied subjects. The Bible is a fascinating book and must be taken as a work of divine inspiration. It then of necessity contains much information, not excluding medical information which is fundamental for all time. The author who examined the Bible from the physician's standpoint could have been clearer in his presentation of the material and omitted much material which is either well-known to the medical reader or easily available to the non-medical reader in any standard textbook. When interpolating medical information the author is not quite up-to-date. Some of the glaring inaccuracies deal with the thymus (status lymphaticus is a frequent finding in cases of sudden death in children), the immunization program in infants and children and scarlet fever (any skin rash should be

considered scarlet fever until proven otherwise). The subject matter of this book deserves a more profound approach.

MICHAEL A. BRESCIA, M.D.

A MANUAL OF CEREBRAL PALSY EQUIPMENT. Paper. Pp. 127. Illustrated. Chicago: The National Society for Crippled Children and Adults, Inc., 1950.

This manual is a must for anyone or group of individuals who attempt to treat the cerebral palsied child. It contains many fine pictures and diagrams of the protean and varied equipment necessary for the treatment and education of the handicapped child. The manual has many fine suggestions for equipment which would give any carpenter a field day. MICHAEL A. BRESCIA, M.D.

ANTIHISTAMINES, INDUSTRY AND PRODUCT SURVEY. By N. Wishnefsky. Paper. Pp. 157. Price $5.00. New York: Chemonomics, Inc., 1950.

This book is primarily of interest to the chemist, especially of the pharmaceutical houses. The various antihistamines and their formulae are given in detail with a brief statement of the activity both therapeutic and toxic. A sketchy and brief history of allergy is made, the antihistamines are traced from Fourneau's work on the dioxanes. A comparative study of the various antihistamines is made and it appears that the best results are obtained in urticaria with least effectiveness in bronchial asthma. Much time is given over to cold cures (oral, topical and hypodermic) with the observation that none have proved of value. This then introduces us to the antihistamine approach to the subject which is most enthusiastically hailed at the outset only to end the discussion with the statement that spontaneous recovery of about a third of the subjects must be born in mind before enthusiastic conclusions are reached. There is little new in this book for the physician.

H. FRUCHTER, M.D.

ENDOCRINE DISORDERS IN CHILDHOOD AND ADOLESCENCE. By Lawson Wilkins, M.D. Cloth. Pp. 408. Illustrated. Price $13.00. Springfield, Illinois: Charles C. Thomas, 1950.

This volume is essentially practical in its approach to the diagnosis and treatment of the endocrine problem. Particular emphasis has been laid on differential diagnosis and the newer diag-

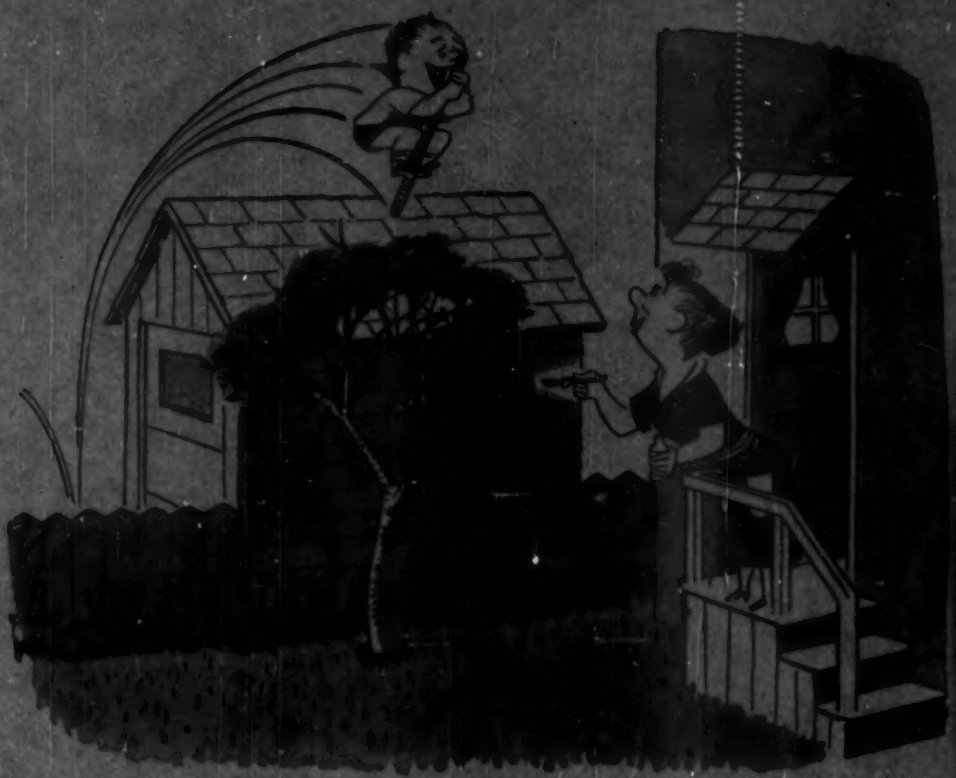
nostic methods clearly outlined. The importance of utilizing these is stressed since some endocrinopathies can be helped by treatment, but the diagnosis must be established without the error of branding the case as an endocrine disorder when it is simply a constitutional variation in the developmental pattern. Incidentally, this 408 page book with its 411 illustrations, is a beautiful example of the book-makers' art. It should prove a boon to the pediatrician in his practice.

J. F. L.

TOM CULLEN OF BALTIMORE. By Judith Robinson. Cloth. Pp. 435. Illustrated. New York: Oxford University Press, 1949.

This biography concerns itself with a well-known figure in medical circles, especially in the field of gynecology. It might be argued that Cullen is a well-known figure in fields other than medicine considering the active part he has taken in civic affairs, in Baltimore and environs, anyway. This biography is peculiar in that the subject of the biography takes an active part in the writing of the book by injecting comments throughout the book. This reviewer feels that this sort of "over the shoulder" writing makes the book less interesting and at times disconcerting and disconnected. The first part of the book, which deals with the early life of Cullen, is most interesting and gives good insight into the quality of the man. However, after Cullen begins his internship, the book becomes most impersonal and tumors and Johns Hopkins Hospital come to the fore out of all proportion. The development of any institution is always fraught with difficulty, personal interests and animosities but such lengthy discussion of these difficulties at Johns Hopkins Hospital has only limited interest. Very little if any of Cullen's personal life or that material which is essential to a good biography is lacking from the point that he begins his internship onward. The book ends on what I believe to be a distasteful note. It depicts a scene in the operating room in which the mighty Cullen is operating and calls on one of a group of fourth year medical students for quizzing as the operation progresses. The only comment that I could make from this scene is that it is either entirely fictitious or the fourth year medical students at Johns Hopkins are poorly trained. The book is disappointing. Cullen deserves better treatment and possibly an independent biographer would do better.

MICHAEL A. BRESCIA, M.D.



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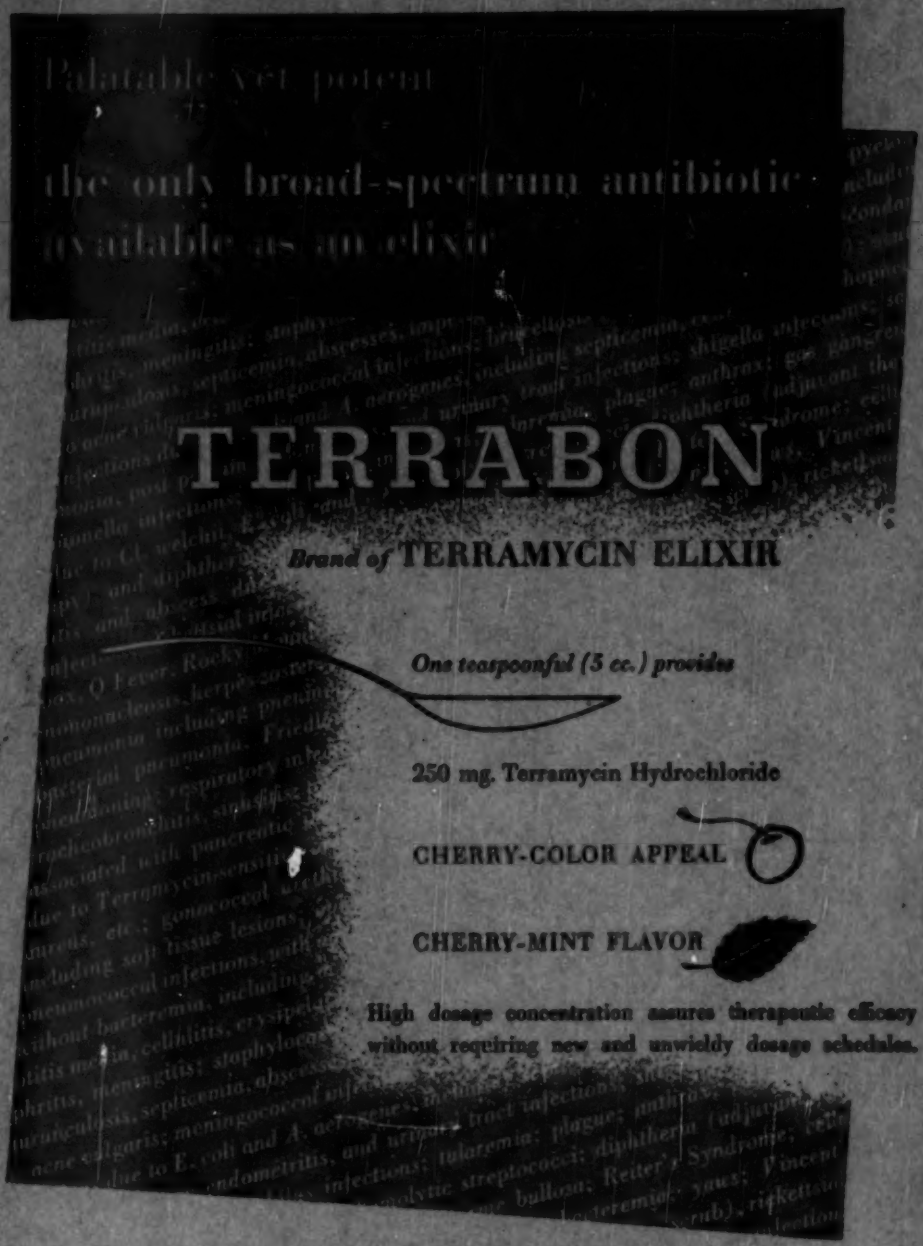
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